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EXAMINER	
GUSSOW, ANNE	

ART UNIT	PAPER NUMBER
1643	

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10/31/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	Application No. 10/672,278	Applicant(s) GOLDENBERG ET AL.	
	Examiner Anne M. Gussow	Art Unit 1643	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 13 September 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,3-6,8,9,14-16,29,31,32,34-37,39 and 48-107 is/are pending in the application.
- 4a) Of the above claim(s) 53-76 and 79-107 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-6,8,9,14-16,29,31,32,34-37,48-52,77 and 78 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 May 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/17/06</u> .  | 6) <input type="checkbox"/> Other: _____                          |

### DETAILED ACTION

1. Applicant's election without traverse of Group I, claims 1 3-52, 77, and 78, in the reply filed on August 24, 2007 is acknowledged.

2. Applicant's election with traverse of species apoptotic drugs, RNase, and DOTA-D-Phe-D-Lys(HSG)-D-Tyr-D-Lys(HSG)-D-Lys(Tscg-Cys)-NH<sub>2</sub> in the reply filed on August 24, 2007 is acknowledged. The traversal is on the ground(s) that the elected species relating to the targetable constructs share common structural and functional characteristics and/or are obvious variants of each other. Upon further consideration, the species election between the targetable conjugated molecules is withdrawn. The species elections between the drugs and toxins remain.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 53-76 and 79-107 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on August 24, 2007.

4. Claims 2, 7, 10-13, 17-28, 30, 33, 38, and 40-47 have been cancelled.

Claims 1, 3-6, 8, 9, 15, 16, 29, 31, 32, 34-37, 39, 48-52, 59, 63, 65, 75, 77, 78, 80, 83, and 107 have been amended.

5. Claims 1, 3-6, 8, 9, 14-16, 29, 31, 32, 34-37, 39, 48-52, 77, and 78, the drug species of apoptotic drugs, and the toxin species of RNase are under examination.

***Information Disclosure Statement***

6. The information disclosure statement (IDS) submitted on November 17, 2006 has been fully considered by the examiner and an initialed copy of the IDS is included with the mailing of this Office Action.

***Specification***

7. The disclosure is objected to because of the following informalities: the specification contains typographical and grammatical errors. For example, in paragraph 31 the phrase "the method a method of treating" and in paragraph 134 the addresses of the ATCC and Gibco/BRL are incorrect.

Appropriate correction is required for all errors throughout.

8. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

9. The use of the trademarks PER.C6®, SuperScript™, and Centricon™ have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The trademark symbols have not been included for the trademarks in this application. Appropriate correction is required for all trademarks throughout.

#### ***Claim Rejections - 35 USC § 112***

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 3-6, 8, and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 recites the limitation "MN-3" in line 2. There is insufficient antecedent basis for this limitation in the claim.

For purposes of this office action it is presumed that the MN-antibody in claim 1 is a typographical error and should read MN-3 because in the claim set filed on August 24, 2007 claim 1 read MN-3 and claim 1 is not listed as amended in the claim set filed on September 13, 2007. Therefore, claim 1 is being interpreted to be a chimeric or humanized MN-3 antibody or fragment that binds NCA90.

12. Claims 1, 3-6, 8, 9, 14-16, 29, 31, 32, 34-37, 39, 48-52, 77, and 78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a.) Claims 1, 3-6, 8, 9, 14-16, 29, 31, 32, 34-37, 39, 48-52, 77, and 78 are vague and indefinite in the recitation of "MN-3" as the sole means of identifying the antibody referred to in claim 1. The use of laboratory designations to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. This rejection can be obviated by amending the claims to specifically and uniquely identify MN-3, for example, by SEQ ID NO.

b.) Claims 3-6, 8, 9, 14-16, 29, 31, 32, 34-37, 39, 48-52, 77, and 78 are vague and indefinite in the recitation of "chimeric" in claim 1 when read with the limitations of the dependent claims. The standard definition of a chimeric antibody is "antibodies that have e.g. mouse Fv fragments for the antigen-binding portion of the molecule, but Fc regions of human Ig which convey effector functions" (Illustrated Dictionary of Immunology, 1995. page 65). Thus, the constant regions of the chimeric antibody are human. It is not clear from the claims, nor applicant's definition of chimeric in the specification (paragraph 105), whether the framework regions of the claimed antibody are human or rodent residues. For example, in claim 4 the framework regions are

human, which defines the antibody as humanized but in claim 3 the limitation of the murine CDR sequences in the absence of specific framework residues would define the antibody as a chimeric antibody.

***Claim Rejections - 35 USC § 102***

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 1, 3-6, 8, 9, 14-16, 29, 31, 34-37, 39, and 48-52 are rejected under 35 U.S.C. 102(a, e) as being anticipated by Goldenberg, et al. (US PAT 6,759,045, PG PUB printed February 21, 2002) as evidenced by Hansen, et al. (Cancer, 1993. Vol. 71, pages 3478-3485) and Becker, et al. (Journal of Nuclear Medicine, 1994. Vol. 35, pages 1436-1443).

The claims recite a chimeric or humanized MN-antibody or fragment thereof that binds NCA90, comprising the MN-3 light chain CDR sequences CDR1 (RSSQSIVHSNGNTYLE, SEQ ID NO: 1), CDR2 (KVSNRFS, SEQ ID NO:2) and CDR3

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(FQGSHVPPT, SEQ ID NO:3) and the MN-3 heavy chain CDR sequences CDR1 (NYGMN, SEQ ID NO:4), CDR2 (WINTYTGEPTYADDFKG, SEQ ID NO:5) and CDR3 (KGWMDFNSSLDY, SEQ ID NO:6), wherein the antibody or fragment is a humanized antibody or fragment comprising the framework (FR) region sequences of the light and heavy chain variable regions of a human antibody and at least one light and heavy chain constant regions of a human antibody, wherein at least one of the FRs of the light and heavy chain variable regions of the humanized MN-3 antibody or fragment thereof comprises at least one amino acid substituted with the corresponding amino acid of the murine MN-3 antibody, wherein the at least one amino acid from the murine MN3 antibody is selected from the group consisting of amino acid residue 27, 30, 67, 68, 69 and 94 of the murine MN-3 heavy chain variable region sequence or amino acid residue 20, 22, 39, 60, 70 and 100 of the murine MN-3 light chain variable region sequence, wherein the antibody or fragment thereof comprises the amino acid sequences of cMN-3VK (SEQ ID NO: 13) and cMN- 3VH (SEQ ID NO:15), wherein the antibody or fragment thereof comprises the amino acid sequences of hMN-3VK (SEQ ID NO: 18) and hMN- 3VH (SEQ ID NO:21), wherein the fragment is selected from the group consisting of Fv, F(ab')<sub>2</sub>, Fab' and Fab, bound to at least one diagnostic/detection agent or at least one therapeutic agent or is part of a fusion protein, wherein the diagnostic/detection agent comprises a photoactive diagnostic/detection agent, a chromagen or dye, a radionuclide with an energy between 20 and 10,000 keV, a gamma-, beta- or a positron- emitting isotope, a contrast agent, a paramagnetic ion, an ultrasound-enhancing agent, a liposome or a radiopaque compound, wherein the



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therapeutic agent is selected from the group consisting of a radionuclide, boron, gadolinium or uranium atoms, an immunomodulator, a cytokine, a hormone, a hormone antagonist, an enzyme, an enzyme inhibitor, a photoactive therapeutic agent, a cytotoxic drug, a toxin, an angiogenesis inhibitor, a different antibody and a combination thereof, wherein the drug is apoptotic, wherein the toxin is ribonuclease (RNase), wherein the immunomodulator is selected from the group consisting of a cytokine, a stem cell growth factor, a lymphotoxin, a hematopoietic factor, a colony stimulating factor (CSF), an interferon (IFN), a stem cell growth factor, erythropoietin, thrombopoietin, an antibody and a combination thereof, wherein the lymphotoxin is tumor necrosis factor (TNF), the hematopoietic factor is an interleukin (IL), the colony stimulating factor is granulocyte-colony stimulating factor (G-CSF) or granulocyte macrophage-colony stimulating factor (GM-CSF)), the interferon is interferons- $\alpha$ , - $\beta$  or - $\gamma$  and the stem cell growth factor designated "S1 factor", wherein the cytokine is selected from the group consisting of IL-1, IL-2, IL-3, IL-6, IL-10, IL-12, IL-18, IL-21, interferon- $\gamma$ , TNF- $\alpha$  and a combination thereof, wherein the radionuclide is selected from the group consisting of P-32, P-33, Sc-47, Fe-59, Cu-64, Cu-67, Se-75, As-77, Sr-89, Y-90, Mo-99, Rh-105, Pd-109, Ag-111, I-125, I-131, Pr-142, Pr-143, Pm-149, Sm-153, Tb-161, Ho-166, Er-169, Lu-177, Re-186, Re-188, Re-189, Ir-194, Au-198, Au-199, Pb-211, Pb-212, and Bi-213, Co-58, Ga-67, Br-80m, Tc-99m, Rh-103m, Pt-109, In-111, Sb-119, I-125, Ho-161, Os-189m, Ir-192, Dy-152, At-211, Bi-212, Ra-223, Rn-219, Po-215, Bi-211, Ac-225, Fr-221, At-217, Fm-255 and combinations thereof.

The claims also recite an antibody fusion protein comprising a first antibody or fragment according to claim 1, attached to a second antibody or fragment, wherein the second antibody or fragment is an antibody or fragment according to claim 1, wherein the second antibody or fragment binds to an antigen other than NCA90, further comprising a diagnostic/detection or therapeutic agent conjugated to the fusion protein, wherein the second antibody or fragment binds to a granulocyte-associated antigen.

Goldenberg, et al. teach an MN-3 antibody which binds to NCA-90 (column 6 lines 60-65), is chimeric or humanized (column 3 lines 65-68) and is a conjugate. Goldenberg, et al. teach the MN-3 antibody can be conjugated to drugs, toxins, chelators, boron addends, or other therapeutic agents (column 9 lines 2-3) including radiolabels (column 12 lines 59- column 13 line 2), immunomodulators (column 13 lines 20-32), toxins (column 13 line 65 through column 14 line 10), chemotherapeutic drugs (column 13 lines 44-55) and photoactive agents or dyes (column 13 lines 56-60). Goldenberg, et al. teach the immunoconjugate fusion protein can be bivalent, trivalent, or tetravalent (column 13 lines 33-37). Hansen, et al. teach that an MN-3 antibody was prepared by immunizing mice with a partially purified CEA preparation (page 3479). Becker, et al. teach that the MN-3 antibody that binds to nonspecific cross-reactive antigen 90 (NCA-90) is a Fab' fragment. Becker, et al. cites the 1993 Hansen, et al. article as the source of the MN-3 antibody. Additionally, the instant specification cites the 1993 Hansen, et al. article as the source of the MN-3 antibody (paragraphs 66 and 67). Since the claims recite an MN-3 antibody and the specification discloses the MN-3 antibody to be derived from the Hansen, et al. antibody, the sequence of the instant

antibody would be an inherent property of the Hansen, et al. antibody. Since, the Goldenberg, et al. patent teaches the humanized or chimeric MN-3 antibody from the same parent antibody as Hansen, et al. all the limitations of the claims have been met.

***Claim Rejections - 35 USC § 103***

15. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 1, 3-6, 8, 9, 14-16, 29, 31, 34-37, 39, 48-52, 77, and 78 are rejected under 35 U.S.C. 103(a) as being obvious over Goldenberg, et al. (US PAT 6,759,045,

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PG PUB printed February 21, 2002) as evidenced by Hansen, et al. (Cancer, 1993. Vol. 71, pages 3478-3485) and Becker, et al. (Journal of Nuclear Medicine, 1994. Vol. 35, pages 1436-1443) in view of Hansen, et al. (US PG PUB 2002/0006379, filed April 3, 2001).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(I)(1) and § 706.02(I)(2).

Claims 1, 3-6, 8, 9, 14-16, 29, 31, 34-37, 39, and 48-52 have been described *supra*. Claims 77-78 recite a kit useful for treating or identifying diseased tissues in a subject comprising: (A) a bi-specific antibody or antibody fragment having at least one

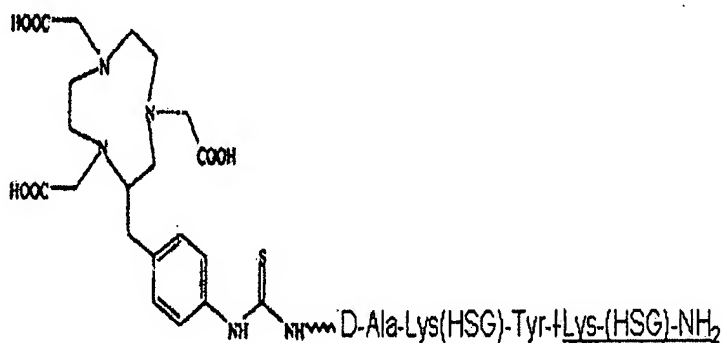
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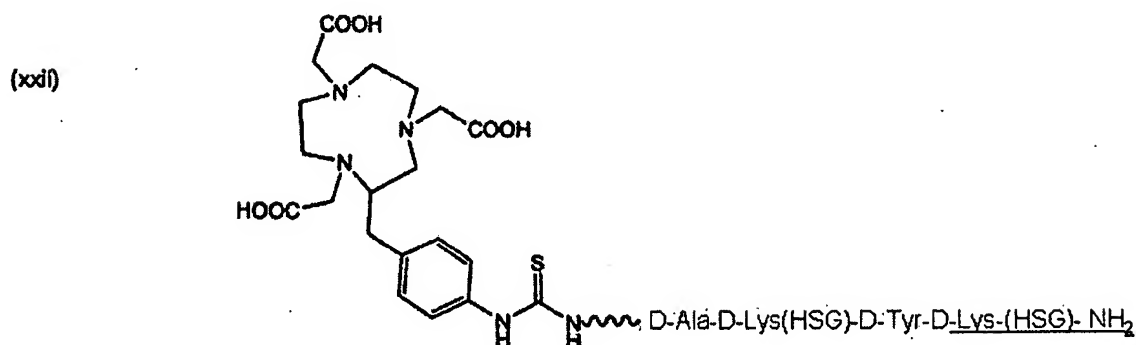
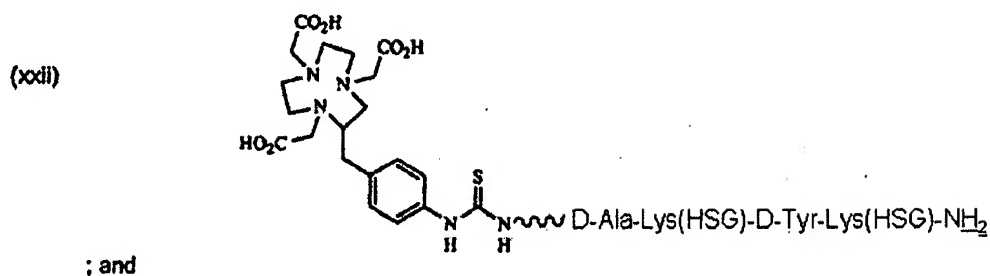
arm that specifically binds a targeted tissue and at least one other arm that specifically binds a targetable conjugate, wherein the one arm that specifically binds a targeted tissue is an antibody or fragment thereof according to claim 3; (B) a first targetable conjugate which comprises a carrier portion which comprises or bears at least one epitope recognizable by the at least one other arm of the bi-specific antibody or antibody fragment, and one or more conjugated therapeutic or diagnostic agents; and (C) optionally, a clearing composition useful for clearing non-localized antibodies and antibody fragments; and (D) optionally, when the therapeutic agent conjugated to the first targetable conjugate is an enzyme, (i) a prodrug, when the enzyme is capable of converting the prodrug to a drug at the target site; or (ii) a drug which is capable of being detoxified in the subject to form an intermediate of lower toxicity, when the enzyme is capable of reconvertng the detoxified intermediate to a toxic form, and, therefore, of increasing the toxicity of the drug at the target site, or (iii) a prodrug which is activated in the subject through natural processes and is subject to detoxification by conversion to an intermediate of lower toxicity, when the enzyme is capable of reconvertng the detoxified intermediate to a toxic form, and, therefore, of increasing the toxicity of the drug at the target site, or (iv) a second targetable conjugate which comprises a carrier portion which comprises or bears at least one epitope recognizable by the at least one other arm of the bi-specific antibody or antibody fragment, and a prodrug, when the enzyme is capable of converting the prodrug to a drug at the target site, wherein the targetable conjugate is selected from the group consisting of (i) DOTA-Phe-Lys(HSG)-D-Tyr-Lys(HSG)-NH<sub>2</sub>; (ii) DOTA-Phe-Lys(HSG)-Tyr-Lys(HSG)-NH<sub>2</sub>

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(SEQ ID NO: 7); (iii) Ac-Lys(HSG)-D-Tyr-Lys(HSG)-Lys(Tscg- Cys)-NH<sub>2</sub>; (iv) DOTA-D-Asp-D-Lys(HSG)-D-Asp-D-Lys(HSG)-NH<sub>2</sub>; (v) DOTA-D-Glu-D- Lys(HSG)-D-Glu-D-Lys(HSG)-NH<sub>2</sub>; (vi) DOTA-D-Tyr-D-Lys(HSG)-D-Glu-D-Lys(HSG)- NH<sub>2</sub>; (vii) DOTA-D-Ala-D-Lys(HSG)-D-Glu-D-Lys(HSG)-NH<sub>2</sub>; (viii) DOTA-D-Phe-D- Lys(HSG)-D-Tyr-D-Lys(HSG)-NH<sub>2</sub>; (ix) Ac-D-Phe-D-Lys(DOTA)-D-Tyr-D-Lys(DOTA)- NH<sub>2</sub>; (x) Ac-D-Phe-D-Lys(DTPA)-D-Tyr-D-Lys(DTPA)-NH<sub>2</sub>; (xi) Ac-D-Phe-D-Lys(Bz- DTPA)-D-Tyr-D-Lys(Bz-DTPA)-NH<sub>2</sub>; (xii) Ac-D-Lys(HSG)-D-Tyr-D-Lys(HSG)-D-Lys(Tscg- Cys)-NH<sub>2</sub>; (xiii) DOTA-D-Phe-D-Lys(HSG)-D-Tyr-D-Lys(HSG)-D-Lys(Tscg-Cys)-NH<sub>2</sub>; (xiv) (Tscg-Cys)-D-Phe-D-Lys(HSG)-D-Tyr-D-Lys(HSG)-D-Lys(DOTA)-NH<sub>2</sub>; (xv) Tscg-D-Cys-D-Glu-D-Lys(HSG)-D-Glu-D-Lys(HSG)-NH<sub>2</sub>; (xvi) (Tscg-Cys)-D-Glu-D-Lys(HSG)-D-Glu-D- Lys(HSG)-NH<sub>2</sub>; (xvii) Ac-D-Cys-D-Lys(DOTA)-D-Tyr-D-Ala-D-Lys(DOTA)-D-Cys-NH<sub>2</sub>; (xviii) Ac-D-Cys-D-Lys(DTPA)-D-Tyr-D-Lys(DTPA)-NH<sub>2</sub>; (xix) Ac-D-Lys(DTPA)-D-Tyr-D- Lys(DTPA)-D-Lys(TscG-Cys)-NH<sub>2</sub>; (xx) Ac-D-Lys(DOTA)-D-Tyr-D-Lys(DOTA)-D- Lys(TscG-Cys)-NH<sub>2</sub>;

(xxi)





Goldenberg, et al. has been described supra. Goldenberg, et al. teach a humanized or chimeric MN-3 antibody that binds to NCA-90. Goldenberg, et al. does not teach a kit comprising an antibody conjugated to a targetable conjugate. This deficiency is made up for in the teachings of Hansen, et al. 2001.

Hansen, et al. teach an kit comprising an antibody conjugate wherein the MN-14 antibody is conjugated to targetable conjugates including DOTA-Phe-Lys(HSG)-D-Tyr-Lys(HSG)-NH<sub>2</sub>; DOTA-Phe-Lys(HSG)-Tyr-Lys(HSG)-NH<sub>2</sub>; Ac-Lys(HSG)D-Tyr-Lys(HSG)-Lys(Tscg-Cys)-NH<sub>2</sub>. Hansen, et al. also teach the incorporation of unnatural amino acids, for example D-amino acids, into the peptide backbone (paragraph 96).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the MN-3 antibody of Goldenberg, et al. conjugated to a targetable conjugate in a kit as taught by Hansen, et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced the antibody of Goldenberg, et al. with a targetable conjugate in a kit as taught by Hansen, et al. because Hansen, et al. teach that the antibodies in the construct can be specific to a variety of cell surface or intracellular tumor antigens (paragraph 135) and that an advantage of a bispecific antibody that is reactive to a targetable construct is the same antibody can be used in a variety of therapeutic and diagnostic applications (paragraph 87). Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the antibody of Goldenberg, et al. with a targetable conjugate in a kit in view of Hansen, et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made, as evidenced by the references.

18. Claims 1, 3-6, 8, 9, 14-16, 29, 31, 34-37, 39, and 48-52 are rejected under 35 U.S.C. 103(a) as being obvious over as being anticipated by Goldenberg, et al. (US PAT 6,759,045, PG PUB printed February 21, 2002) as evidenced by Hansen, et al. (Cancer, 1993. Vol. 71, pages 3478-3485) and Becker, et al. (Journal of Nuclear Medicine, 1994. Vol. 35, pages 1436-1443) in view of Orlandi et al (Proc. Natl. Acad.



Sci. USA, 86:3833-3837, 1989), Cabilly et al (U.S Patent 4816567, issued 3/89), Boss et al (U.S Patent 4816397, issued 3/89), Robinson et al (U.S. Patent 5618920, filed 4/94), Ward et al (Nature 341:544-546, 1989), and Huston et al (U.S. Patent 5258498, issued 11/93).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(I)(1) and § 706.02(I)(2).

The claims have been described supra.

Goldenberg, et al. has been described supra. Goldenberg, et al. teach a humanized or chimeric MN-3 antibody that binds to NCA-90. Goldenberg, et al. do not teach the sequence of the MN-3 antibody. This deficiency is made up for in the

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teachings of Orlandi, et al., Robinson, et al., Ward, et al., Cabilly, et al., Boss, et al., and Huston, et al.

Orlandi et al teach a general method for obtaining the VH and the VL genes and the amino acid sequence of an antibody by PCR from the hybridoma cell. Orlandi also teaches primers and the use of said primers to clone DNA encoding murine variable heavy regions (see page 3833 and 3834) and the method obtained the sequences for five of the hybridomas for which it was applied.

Robinson et al (see columns 12-22) and Ward et al (see entire document) teach Fv derived from a known antibody. Robinson et al teach Fv, determination of nucleic acids encoding VH and VL of any known antibody and use of said VH and VL to produce FV (see column 1-45, and columns 12-22). Robinson et al teach that "The invention also produces consensus sequences and specific oligonucleotide sequences useful as probes for hybridization and priming cDNA synthesis of any hybridoma mRNA coding for variable regions of any desired specificity." (see column 4, last paragraph). Ward et al teach vectors for producing FV.

Both Cabilly et al and Boss et al disclose methods for the determination of nucleic acids encoding VH and VL of any known antibody.

Huston et al teach that the sequence of the VH and VL of a known antibody can be determined by amino acid sequencing and "The 5' end portion of the mRNA can be used to produce the cDNA for subsequent sequencing or the amino acid sequence of the hypervariable and flanking framework regions can be determined by amino acid

sequencing of the V regions of the H and L chains. Such sequence analysis is now conducted routinely".

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the antibody MN-3 and obtain the DNA and protein sequence of the VH and the VL by the method of Orlandi, et al., Cabilly, et al., Boss, et al., Robinson, et al., Ward, et al. and Huston, et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the antibody MN-3 and obtain the DNA and protein sequence of the VH and the VL by the method of Orlandi, et al., Cabilly, et al., Boss, et al., Robinson, et al., and Ward, et al. and Huston, et al. because although the references do not teach the amino acid sequences of the MN-3 antibody, the references cited in this rejection teach FV, nucleic acids encoding VH and VL and the methods of making FV based on the nucleic acid sequence of any known antibody VH and VL, and methods of determining the nucleic acid sequence of any known antibody VH and VL. All Fv are structurally similar in that they contain similar numbers of amino acids organized in a similar fusion (e.g. they contain a VH and VL wherein the VH and VL contain framework and variable region amino acids). Thus it would not have been undue experimentation to obtain SEQ ID Nos. 1-6, 13, 15, 18, or 21 because the art recognizes that hundreds, if not thousands of antibody molecule VH and VL regions have been cloned and sequenced. As taught by Orlandi et al it was routine to obtain the VH and the VL genes from PCR primers from the hybridoma of an antibody and "our primers might amplify most immunoglobulin mRNA of the mouse repertoire" (see page

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3836, right column) and "the teachings should lead to the cloning of antigen-binding specificities directly from immunoglobulin genes" (see abstract, last sentence). Cabilly et al teach that regarding VH and VL nucleic acid sequences that, "the variable regions can conveniently be derived from presently known sources using readily available hybridomas" (see column 6, last paragraph). Robinson et al teach that "The invention also produces consensus sequences and specific oligonucleotide sequences useful as probes for hybridization and priming cDNA synthesis of any hybridoma mRNA coding for variable regions of any desired specificity." (see column 4, last paragraph). Huston et al teach "The invention also produces consensus sequences and specific oligonucleotide sequences useful as probes for hybridization and priming cDNA synthesis of any hybridoma mRNA coding for variable regions of any desired specificity." (see column 4, last paragraph). Thus, the art recognized that there was a reasonable expectation of success that the nucleic acid sequence of the VH and VL of the art known MN-3 antibody could be established using techniques disclosed in the references used in the instant rejection. As evidenced by Becker, et al. the MN-3 antibody is a mouse IgG1 produced by a hybridoma cell (see page 1438). One of ordinary skill in the art would reasonably conclude that Hansen et al's antibody also possesses the same VH and VL of the instant antibody; therefore, it appears that Goldenberg et al's would have the same VH and VL sequences of the instant application. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed antibody with the antibody of Goldenberg, et al, the burden of proof is upon the Applicants to show an unobvious distinction between the

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structural and functional characteristics of the claimed antibody and the antibody of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

### ***Conclusion***

19. No claims are allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571) 272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

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USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow

October 24, 2007

A handwritten signature in black ink, appearing to be 'L. Helms', written in a cursive style.

**LARRY R. HELMS, PH.D.**  
**SUPERVISORY PATENT EXAMINER**